

Robert Greene Sterne
Edward J. Kessler
Jorge A. Goldstein
David K.S. Commwell
Robert W. Esmond
Tracy-Gene G. Durkin
Michele A. Cimbala
Michael B. Ray
Robert E. Sokohl
Eric K. Steffe
Michael Q. Lee
Steven R. Ludwig
John M. Covert
Linda E. Alcorn
Robert C. Millonig
Lawrence B. Bugaisky
Donald J. Featherstone
Michael V. Messinger

Judith U. Kim
Timothy J. Shea, Jr.
Patrick E. Garrett
Heidi L. Kraus
Edward W. Yee
Albert L. Ferro*
Donald R. Banowitz
Peter A. Jackman
Molly A. McCall
Teresa U. Medler
Jeffrey S. Weaver
Kendrick P. Patterson
Vincent L. Capuano
Eldora Ellison Floyd
Thomas C. Fiala
Brian J. Del Buono
Virgil Lee Beaton
Kimberly N. Reddick

Theodore A. Wood
Elizabeth J. Haanes
Bruce E. Chalker
Joseph S. Ostroff
Frank R. Cottingham
Christine M. Uhulier
Rae Lynn Pngamam
Jane Shershenovich*
Lawrence J. Carroll*
George S. Bardmesser
Daniel A. Klein*
Rodney G. Maze
Jason D. Eisenberg
Michael D. Specht
Andrea J. Kamage
Tracy L. Muller*
Jon E. Wright*
LuAnne M. Yuricek*

John J. Figueroa
Ann E. Summerfield
Registered Patent Agents*
Karen R. Markowicz
Nancy J. Leith
Helene C. Carlson
Gaby L. Longworth
Matthew J. Dowd
Aaron L. Schwartz
Angelique G. Uy
Mary B. Tung
Katrina Y. Pei
Bryan L. Skelton
Robert A. Schwartzman
Timothy A. Doyle
Jennifer R. Mahalingappa

Teresa A. Colella
Jeffrey S. Lundgren
Victoria S. Rutherford
Eric D. Hayes

Of Counsel
Kenneth C. Bass III
Evan R. Smith

*Admitted only in Maryland
*Admitted only in Virginia
*Practice Limited to
Federal Agencies

October 10, 2003

WRITER'S DIRECT NUMBER:
(202) 772-8589

INTERNET ADDRESS:
LARRYB@SKGF.COM

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Art Unit To be assigned

Re: U.S. Utility Patent Application
Appl. No. 10/602,045; Filed: June 24, 2003
For: **Molecular Detection Systems Utilizing Reiterative Oligonucleotide
Synthesis**
Inventors: Michelle M. Hanna
Our Ref: 2072.0010003/LBB/SJE

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Second Supplemental Information Disclosure Statement;
2. Form PTO-1449 (9 sheets citing 31 documents); and
3. One (1) return postcard.

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

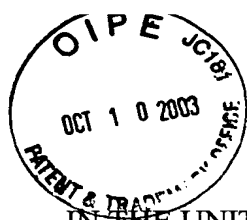
Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Lawrence B. Bugaisky
Attorney for Applicant
Registration No. 35,086

LBB/SJE/lam
Enclosures

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Michelle M. HANNA

Appl. No. 10/602,045

Filed: June 24, 2003

For: **Molecular Detection Systems
Utilizing Reiterative
Oligonucleotide Synthesis**

Confirmation No. *To be assigned*

Art Unit: *To be assigned*

Examiner: *To be assigned*

Atty. Docket: 2072.0010003/LBB/SJE

Second Supplemental Information Disclosure Statement

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. The numbering on this Second Supplemental Information Disclosure Statement is a continuation of the numbering in Applicant's First Supplemental Information Disclosure Statement filed on August 12, 2003, in connection with the above-captioned application. Copies of the cited documents were cited by or submitted to the Office in Information Disclosure Statements that comply with 37 C.F.R. § 1.98(a)-(c) in Application No. 09/984,664, filed October 30, 2001, which is relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of these documents are not attached. 37 C.F.R. § 1.98(d).

The Examiner is referred to the following list of related, co-pending patent applications:

International Application PCT/US02/3419, filed October 29, 2002, which designates the United States and was published in English on May 8, 2003 as WO 03/038942 A2, listed as document **AM1**; and

U.S. Patent Application No. 10/425,037, filed April 29, 2003.

The Examiner is also referred to the following list of related, co-pending patent applications which contain the identical specification as the present application:

U.S. Patent Application No. 09/984,664, filed October 30, 2001;

U.S. Patent Application No. 10/600,581, filed June 23, 2003; and

U.S. Patent Application No. 10/607,136, filed June 27, 2003.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicant has listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

Applicant reserves the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith.

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Lawrence B. Bugaisky
Attorney for Applicant
Registration No. 35,086

Date: October 19, 2003
1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600



FORM PTO-1449

**SECOND SUPPLEMENTAL
INFORMATION DISCLOSURE STATEMENT**ATTY. DOCKET NO.
2072.0010003/LBB/SJEAPPLICATION NO.
10/602,045APPLICANT
Michelle HannaFILING DATE
June 24, 2003GROUP
To be assigned**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
	AC						
	AD3	5,571,669	11/05/1996	Lu et al.			01/14/1993
	AE3	6,251,594 B1	06/26/2001	Gonzalzo et al.			06/09/1998
	AF3	2003/0099950 A1	05/29/2003	Hanna, M.M.			10/30/2001
	AG						
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FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	WO 89/01050	02/09/1989	WIPO			Yes No
	AM1	WO 03/038042 A2	05/08/2003	WIPO			Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

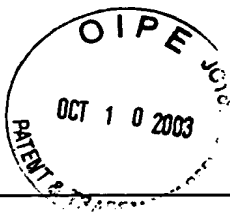
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR		
	AS	<u>12</u>	Antequerra, F., and Bird, A., "Number of CpG islands and genes in human and mouse," <i>Proc. Natl. Acad. Sci. USA</i> 90:11995-11999, National Academy of Sciences (1993).
	AT	<u>12</u>	Callahan, R., et al., "Frequent Mutations in Breast Cancer," <i>Ann. N.Y. Acad. Sci.</i> 698:21-30, New York Academy of Sciences (1993).

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



FORM PTO-1449 SECOND SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT	ATTY. DOCKET NO. 2072.0010003/LBB/SJE	APPLICATION NO. 10/602,045
	APPLICANT Michelle Hanna	
	FILING DATE June 24, 2003	GROUP To be assigned

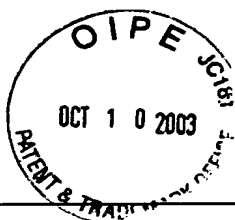
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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	<u>13</u>	Cifone, M.A., and Fidler, I.J., "Increasing metastatic potential is associated with increasing genetic instability of clones isolated from murine neoplasms," <i>Proc. Natl. Acad. Sci. USA</i> 78:6949-6952, National Academy of Sciences (1981).	
AS	<u>13</u>	Esteller, M., et al., "Promoter Hypermethylation and BRCA1 Inactivation in Sporadic Breast and Ovarian Tumors," <i>J. Natl. Cancer Inst.</i> 92:564-569, Oxford University Press (April 2000). (Retrieved from LexisNexis Academic database)	
AT	<u>13</u>	Frommer, M., et al., "A genomic sequencing protocol that yields a positive display of 5-methylcytosine residues in individual DNA strands," <i>Proc. Natl. Acad. Sci. USA</i> 89:1827-1831, National Academy of Sciences (1992).	

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FORM PTO-1449 <u>SECOND SUPPLEMENTAL</u> <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 2072.0010003/LBB/SJE	APPLICATION NO. 10/602,045
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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	<u>14</u>	Giusti, W.G., and Adriano, T., "Synthesis and Characterization of 5'-Fluorescent-dye-labeled Oligonucleotides," <i>PCR Methods Appl.</i> 2:223-227, Cold Spring Harbor Laboratory Press (1993).	
AS	<u>14</u>	Gupta, K.C., et al., "A general method for the synthesis of 3'-sulfhydryl and phosphate group containing oligonucleotides," <i>Nucleic Acids Res.</i> 19:3019-3025, Oxford University Press (1991).	
AT	<u>14</u>	Herman, J.G., et al., "Inactivation of the <i>CDKN2/p16/MTS1</i> Gene Is Frequently Associated with Aberrant DNA Methylation in All Common Human Cancers," <i>Cancer Res.</i> 55:4525-4530, American Association for Cancer Research (1995).	

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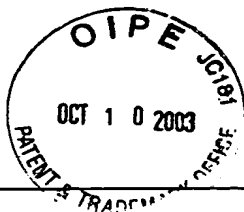
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	15	Herman, J.G., et al., "Incidence and functional consequences of hMLH1 promoter hypermethylation in colorectal carcinoma," <i>Proc. Natl. Acad. Sci. USA</i> 95:6870-6875, National Academy of Sciences (1998).	
AS	15	Horii, A., et al., "Frequent Replication Errors at Microsatellite Loci in Tumors of Patients with Multiple Primary Cancers," <i>Cancer Res.</i> 54:3373-3375, American Association for Cancer Research (1994).	
AT	15	Issa, J.-P.J., et al., "Methylation of the oestrogen receptor CpG island links ageing and neoplasia in human colon," <i>Nat. Genet.</i> 7:536-540, Nature Publishing Co. (1994).	

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	<u>16</u>	Jin, D.J., "An <i>Escherichia coli</i> RNA Polymerase Defective in Transcription due to its Overproduction of Abortive Initiation Products," <i>J. Mol. Biol.</i> 236:72-80, Academic Press Limited (1994).	
AS	<u>16</u>	Langer, P.R., et al., "Enzymatic synthesis of biotin-labeled polynucleotides: Novel nucleic acid affinity probes," <i>Proc. Natl. Acad. Sci. USA</i> 78:6633-6637, National Academy of Sciences (1981).	
AT	<u>16</u>	Loeb, L.A., "Mutator Phenotype May Be Required for Multistage Carcinogenesis," <i>Cancer Res.</i> 51:3075-3079, American Association for Cancer Research (1991).	

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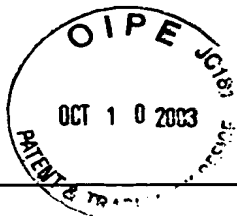
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>17</u>	Meinkoth, J., and Wahl, G., "Hybridization of Nucleic Acids Immobilized on Solid Supports," <i>Anal. Biochem.</i> 138:267-284, Academic Press, Inc. (1984).
	AS	<u>17</u>	Nowell, P.C., "The Clonal Evolution of Tumor Cell Populations," <i>Science</i> 194:23-28, American Association for the Advancement of Science (1976).
	AT	<u>17</u>	Palmisano, W.A., et al., "Predicting Lung Cancer by Detecting Aberrant Promoter Methylation in Sputum," <i>Cancer Res.</i> 60:5954-5958, American Association for Cancer Research (November 2000).

EXAMINER

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	APPLICANT Michelle Hanna	
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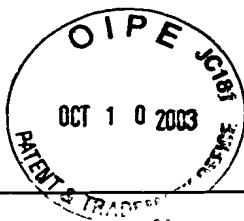
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	<u>18</u>	Radlowski, M., and Job, D., "Effect of disulfide and sulfhydryl reagents on abortive and productive elongation catalyzed by <i>Escherichia coli</i> RNA polymerase," <i>Acta Biochim. Pol.</i> 41:415-419, Panstwowe Wydawnictwo Naukowe (1994).	
AS	<u>18</u>	Rice, J.C., et al., "Aberrant methylation of the <i>BRCA1</i> CpG island promoter is associated with decreased <i>BRCA1</i> mRNA in sporadic breast cancer cells," <i>Oncogene</i> 17:1807-1812, Stockton Press (1998).	
AT	<u>18</u>	Robertson, K.D., "DNA methylation, methyltransferases, and cancer," <i>Oncogene</i> 20:3139-3155, Nature Publishing Group (May 2001).	

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>19</u>	Tlsty, T.D., et al., "Differences in the rates of gene amplification in nontumorigenic and tumorigenic cell lines as measured by Luria-Delbrück fluctuation analysis," <i>Proc. Natl. Acad. Sci. USA</i> 86:9441-9445, National Academy of Sciences (1989).
AS	<u>19</u>	Toyota, M., and Issa, J.-P.J., "CpG island methylator phenotypes in aging and cancer," <i>Semin. Cancer Biol.</i> 9:349-357, Academic Press (1999).
AT	<u>19</u>	Toyota, M., and Issa, J.-P.J., "The role of DNA hypermethylation in human neoplasia," <i>Electrophoresis</i> 21:329-333, Wiley-VCH Verlag GmbH (January 2000).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>20</u>	Vogelstein, B., and Kinzler, K.W., "The multistep nature of cancer," <i>Trends Genet.</i> 9:138-141, Elsevier Science Publishers Ltd. (1993).
	AS	<u>20</u>	Wang, J.-Y., et al., "Monovalent cations differ in their effects on transcription initiation from a σ -70 promoter of <i>Escherichia coli</i> ," <i>Gene</i> 196:95-98, Elsevier Science B.V. (1997).
	AT	<u>20</u>	Wu, D.Y., and Wallace, R.B., "The Ligation Amplification Reaction (LAR) - Amplification of Specific DNA Sequences Using Sequential Rounds of Template-Dependent Ligation," <i>Genomics</i> 4:560-569, Academic Press, Inc. (1989).

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